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| 09/823,648 | 03/30/2001 | David G. Lowe | P1819R1 | 8510 |

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GENENTECH, INC.
1 DNA WAY
SOUTH SAN FRANCISCO, CA 94080

| EXAMINER |
|---|
| CHAKRABARTI, ARUN K |

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17

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. 09/823,648 | Applicant(s) LOWE ET AL. | |
|---|---|---|---|
| | Examiner Arun Chakrabarti | Art Unit 1634 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____ .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) 1-40 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-40 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 13 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Detailed Action* .

## DETAILED ACTION

### *Specification*

1. Claims 41-104 have been canceled without prejudice towards further prosecution. Claims 4, 17, and 25 have been amended.

### *Claim Rejections - 35 USC § 102*

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

3. Claims 1-9, 15-19, 25-27, and 40 are rejected under 35 U.S.C. 102 (a) as being anticipated by Thompson et al. (PCT International Publication Number WO 99/20640) (April 29, 1999).

Thompson et al teach a microarray comprising a surface sialinized with a silane in toluene in the absence of acetone or an alcohol, and a target molecule, wherein the target molecule is attached to the surface via the silane (Abstract, page 17a, line 18 to page 19, line 31, and page 30, line 11 to page 31, line 10 and Claim 1).

Thompson et al teach a microarray comprising a linker, wherein the target molecule is attached to the surface via the linker (Abstract, Claims 3-4 and 11-14 and page 1, lines 11-15 and page 2, line 25 to page 3, line 24).

Thompson et al teach a microarray, wherein the target is a DNA polynucleotide ranging from 3 bp to 10 Kb (Abstract, Claim 10, and page 30, line 11 to page 32, line 15 and page 8, line 32 to page 9, line 25).

Thompson et al teach a microarray, wherein the planar substrate surface is selected from polymeric materials, ceramics, glasses, or glass slides, plates or electrophoretic membranes (Claim 12 and Figures 2-3).

Thompson et al teach a microarray prepared by a method comprising:

a) providing a multi functional linker reagent comprising two or more reactive groups capable of reacting with a functional group on a surface of a microarray substrate and capable of reacting with a target molecule (Abstract, Claims 1-11, and page 8, line 20 to page 9, line 6);

b) activating the substrate surface for immobilizing the target molecule, by silanizing the surface with a silane in toluene in the absence of acetone or an alcohol, wherein the silane comprises a functionally reactive molecule with the multi functional linker reagent , and wherein the activating further comprises immobilizing the multi functional linker reagent on the silanized surface by attaching the multi functional linker reagent to the silane via a first reactive group of the linker reagent and a reactive group of the silane (Abstract, Claims 1-11 and page 9, line 8 to page 11, line 19 and page 17a, line 30 to page 18, line 19);

c) providing a solution comprising a target having one or more functional groups reactive with a second reactive group of the immobilized multi functional linker reagent (page 11, line 20 to page 13, line 29 and claim 17);

d) attaching the target molecule to the substrate surface by contacting the target molecule with the activated substrate surface under conditions that promote attachment of the target molecule to the immobilized multi functional linker reagent (page 13, line 30 to page 15, line 26 and Abstract and Claim 18).

Thompson et al teach a microarray, wherein the target molecule is an unmodified polynucleotide, and wherein the contacting of step (d) is carried out by spotting the polynucleotide on an activated substrate surface (Abstract, figure 3 and 5, and page 43, line 13 to page 46, line 14).

Thompson et al teach a microarray, wherein the microarray further comprises, after step (d), blocking unreacted reactive groups (Claim 16 and page 15, lines 14-16).

***Claim Rejections - 35 USC § 103***

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CAR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 1-9, 15-19, 25-27, and 30-40 are rejected under 35 U.S.C. 103 (a) over Thompson et al. (PCT International Publication Number WO 99/20640) (April 29, 1999).

Thompson et al teach a microarray of claims 1-9, 15-19, 25-27 and 40 as described above.

Thompson et al do not teach the concentration of the polynucleotide spot in the range of 0.1 microgram/microliter to 3 microgram/microliter, and the pH range of attaching step (d) is from 6 to 10 and attaching is allowed from 1-24 hours.

However, it is *prima facie* obvious that selection of the specific polynucleotide spotting concentration, pH range and incubation time for the attaching reaction represents routine optimization with regard to production of desired microarray which routine optimization parameters are explicitly recognized to an ordinary practitioner in the relevant art. As noted *In re Aller*, 105 USPQ 233 at 235,

> More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.

Routine optimization is not considered inventive and no evidence has been presented that the

specific polynucleotide spotting concentration, pH range and incubation time for the attaching reaction selection performed was other than routine, that the products resulting from the optimization have any unexpected properties, or that the results should be considered unexpected in any way as compared to the closest prior art.

6. Claims 1-19, and 25-40 are rejected under 35 U.S.C. 103 (a) over Thompson et al. (PCT International Publication Number WO 99/20640) (April 29, 1999) in view of Dintzis et al. (U.S. Patent 6,340,460 B1) (January 22, 2002).

Thompson et al teach a microarray of claims 1-9, 15-19, 25-27, and 30-40 as described above.

Thompson et al do not teach a microarray comprising a primary amine at the 5' end of the polynucleotide, wherein the primary amine is attached at the 5' end of the polynucleotide via a linker, wherein the linker comprises one or more monomers of 1-20 carbon atoms, and wherein the monomer comprises a linear chain of carbon or rings.

Dintzis et al. teach a microarray comprising a primary amine at the 5' end of the polynucleotide, wherein the primary amine is attached at the 5' end of the polynucleotide via a linker, wherein the linker comprises one or more monomers of 1-20 carbon atoms, and wherein the monomer comprises a linear chain of carbon or rings (Column 15, lines 5-16 and Column 37, lines 48-58).

Thompson et al do not teach a microarray, wherein the polynucleotide is prepared by extending a nucleic acid primer comprising a primary amine at its 5' end.

Dintzis et al. teach a microarray, wherein the polynucleotide is prepared by extending a nucleic acid primer comprising a primary amine at its 5' end (Column 15, lines 5-16 and Column 37, lines 48-58).

It would have been *prima facie* obvious to an ordinary practitioner to combine and substitute a microarray, comprising a primary amine at the 5' end of the polynucleotide, wherein the primary amine is attached at the 5' end of the polynucleotide via a linker, wherein the linker comprises one or more monomers of 1-20 carbon atoms, and wherein the monomer comprises a linear chain of carbon or rings as taught by Dintzis et al. in the microarray of Thompson et al., since Dintzis et al. state, "For general conjugation reactions, introduction of, for example, primary amines onto the scaffold provides a functional group capable of accepting multiple chemical modifications or manipulations that can be achieved using mild conditions in aqueous solutions (Column 15, lines 5-9)." Moreover, Dintzis et al provides further motivation as Dintzis et al state, "As an alternative to the Aminolink approach, this method (of amine incorporation) has the advantage of verification of incorporation of the nucleotide bearing the protected amino group (via standard DNA calorimetric coupling assays) (Column 37, lines 54-58)". An ordinary practitioner would have been motivated to combine and substitute a microarray, comprising a primary amine at the 5' end of the polynucleotide, wherein the primary amine is attached at the 5' end of the polynucleotide via a linker, wherein the linker comprises one or more monomers of 1-

20 carbon atoms, and wherein the monomer comprises a linear chain of carbon or rings as taught by Dintzis et al. in the microarray of Thompson et al. in order to achieve the express advantages, as noted by Dintzis et al. of introduction of primary amines onto the scaffold which provides a functional group capable of accepting multiple chemical modifications or manipulations that can be achieved using mild conditions in aqueous solutions and also to achieve the advantage of verification of incorporation of the nucleotide bearing the protected amino group (via standard DNA calorimetric coupling assays).

7. Claims 1-9, 15-21, 25-27, and 30-40 are rejected under 35 U.S.C. 103 (a) over Thompson et al. (PCT International Publication Number WO 99/20640) (April 29, 1999) in view of Friend et al. (U.S. Patent 6,324,479 B1) (November 27, 2001).

Thompson et al teach a microarray of claims 1-9, 15-19, 25-27, and 30-40 as described above.

Thompson et al do not teach a microarray, wherein the unmodified target molecule is attached after contacting the target molecule with the surface by a technique selected from printing or deposition on mask.

Friend et al. teach a microarray, wherein the unmodified target molecule is attached after contacting the target molecule with the surface by a technique selected from printing or deposition on mask (Column 34, lines 9-67).

It would have been *prima facie* obvious to an ordinary practitioner to combine and substitute a microarray, wherein the unmodified target molecule is attached after contacting the

target molecule with the surface by a technique selected from printing or deposition on mask as taught by Friend et al. in the microarray of Thompson et al., since Friend et al. state, "A preferred method for attaching the nucleic acids to a surface is by printing on glass plates. This method is especially useful for preparing microarrays of cDNA (Column 34, lines 13-17)." An ordinary practitioner would have been motivated to combine and substitute a microarray, wherein the unmodified target molecule is attached after contacting the target molecule with the surface by a technique selected from printing or deposition on mask as taught by Friend et al. in the microarray of Thompson et al. in order to achieve the express advantages, as noted by Friend et al., of a preferred method for attaching the nucleic acids to a surface by printing on glass plates which is especially useful for preparing microarrays of cDNA.

8. Claims 1-19, and 22-40 are rejected under 35 U.S.C. 103 (a) over Thompson et al. (PCT International Publication Number WO 99/20640) (April 29, 1999) in view of Dintzis et al. (U.S. Patent 6,340,460 B1) (January 22, 2002) further in view of Friend et al. (U.S. Patent 6,324,479 B1) (November 27, 2001).

Thompson et al. in view of Dintzis et al teach the microarray of claims 1-19, and 25-40 as described above including the modification of target nucleotide with primary amine.

Thompson et al. in view of Dintzis et al do not teach a microarray, wherein the unmodified target molecule is attached after contacting the target molecule with the surface by a technique selected from printing or deposition on mask.

Friend et al. teach a microarray, wherein the unmodified target molecule is attached after contacting the target molecule with the surface by a technique selected from printing or deposition on mask (Column 34, lines 9-67).

It would have been *prima facie* obvious to an ordinary practitioner to combine and substitute a microarray, wherein the unmodified target molecule is attached after contacting the target molecule with the surface by a technique selected from printing or deposition on mask as taught by Friend et al. in the microarray of Thompson et al in view of Dintzis et al., since Friend et al. state, "A preferred method for attaching the nucleic acids to a surface is by printing on glass plates. This method is especially useful for preparing microarrays of cDNA (Column 34, lines 13-17)." An ordinary practitioner would have been motivated to combine and substitute a microarray, wherein the unmodified target molecule is attached after contacting the target molecule with the surface by a technique selected from printing or deposition on mask as taught by Friend et al. in the microarray of Thompson et al. in view of Dintzis et al in order to achieve the express advantages, as noted by Friend et al., of a preferred method for attaching the nucleic acids to a surface by printing on glass plates which is especially useful for preparing microarrays of cDNA.

***Response to Amendment***

9. In response to amendment, 112 (second paragraph) rejections are hereby withdrawn. However, all 102 (a) and 103 (a) rejections are hereby properly maintained.

***Response to Arguments***

10. Applicant's arguments filed on July 19, 2002 have been fully considered but they are not persuasive. Applicant argues that 102 (a) rejection should be withdrawn because Thompson et al reference does not teach or suggest the main feature of the invention i.e., silanizing in toluene in the absence of acetone or an alcohol. This argument is not persuasive.

Applicant argues that the phrase "absence of acetone or an alcohol" was not found in Thompson reference. Applicant argues that because Thompson has a preferred embodiment of other solvents, Thompson is limited to the preferred embodiment. This argument is not persuasive. As MPEP 2123 states "Disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. In re Susi,169 USPQ 423 (CCPA 1971)." MPEP 2123 also states " A reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including nonpreferred embodiments. Merck & Co. v. Biocraft Laboratories , 10 USPQ2d 1843 (Fed. Cir. 1989)." It is clear that simply because Thompson has a preferred embodiment, this embodiment does not prevent the reference from suggesting broader embodiments in the disclosure and that this does not constitute a teaching away. Although Thompson reference does not explicitly disclose the phrase "absence of acetone or an alcohol", the property of absence of acetone or an alcohol is inherently present in this chemically and structurally identical molecule toluene. Moreover, Thompson teaches explicitly that water miscible solvents are unsuitable for

silanization (Page 18, lines 12-13). Moreover, MPEP 2111 states, "Claims must be given their broadest reasonable interpretation. During patent examination, the pending claims must be "given the broadest reasonable interpretation consistent with the specification". Applicant always has the opportunity to amend the claims during prosecution and broad interpretation by the examiner reduces the possibility that the claim, once issued, will be interpreted more broadly than it is justified. *In re Prater,* 415 F.2d 1393, 1404-05, 162 USPQ 541, 550-51 (CCPA 1969)". In this case, any water miscible solvents like alcohol and acetone (well known in the art as well as to an ordinary practitioner) are inherently considered unsuitable for silanization as evidenced by Thompson reference. Therefore the "absence of acetone or an alcohol" is directly implicated by the teaching of Thompson reference.

Applicant also argues to withdraw 103 (a) reference based on the absence of teaching of "absence of acetone or an alcohol". In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Therefore, all the 102 (a) and 103 (a) rejections made in the first office action are hereby properly maintained.

***Conclusion***

11. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CAR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CAR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti , Ph. D., whose telephone number is (703) 306-5818. The examiner can normally be reached on 7:00 AM-4:30 PM from Monday to Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-7401. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group analyst Chantae Dessau whose telephone number is (703) 605-1237.

**Arun Chakrabarti,**

**Patent Examiner**

**August 2, 2002**